

**Remarks**

Claims 1, 3, 4-9, 11 and 14 are pending in this application. By this Amendment, claim 14 is amended. Support for the amendment to can be found in the specification as originally filed, for example, at page 5, line 25 – page 6, line 10, and in claim 14 as originally filed. No new matter is added by these amendments.

Entry of the amendments is proper under 37 C.F.R. §1.116 because the amendments (a) place the application in condition for allowance for the reasons discussed below, (b) do not raise any new issues that would require further search and/or consideration, (c) do not present any new claims; and (d) place the application in better form for appeal, should appeal be necessary. These amendments are necessary and were not earlier presented because they are made in response to arguments raised in the Final Rejection. Entry of the amendment is thus respectfully requested.

**I. Claim Rejection Under 35 U.S.C. §112 First Paragraph**

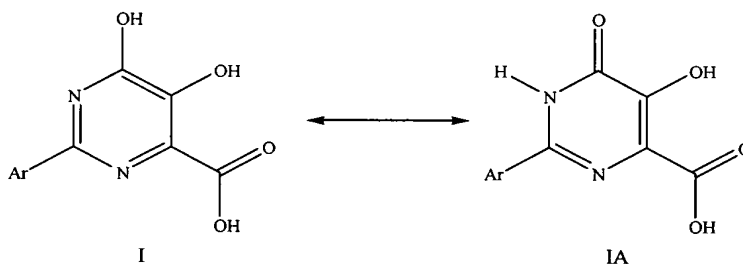
The Office Action rejects claim 14 under 35 U.S.C. §112, first paragraph, because the specification allegedly does not provide enablement for a method of preventing an illness due to hepatitis C virus by administering a prophylactically effective amount of a compound of formula (I). While Applicants do not necessarily agree with this rejection, claim 14 is amended herein. Reconsideration and withdrawal of the rejection are respectfully requested in light of these amendments.

**II. Claim Rejection Under 35 U.S.C. §103(a)**

Claims 1 3-9, 11, 13 and 14 are rejected under 35 U.S.C. §103(a) over International Patent Application Publication No. WO 02/006246 to Gardelli et al.

Independent claim 1, from which claims 3-9, 11 and 14 depend, sets forth, in pertinent part, a "compound of formula (I) below, or a pharmaceutically acceptable salt thereof:

The '246 publication teaches 2-aryl-4,5-dihydroxy-6-carboxypyrimidines of formula I that exist in equilibrium with tautomeric forms such as those of formula IA. *See* '246 publication, page 1, line 25 – page 2, line 12.



The cited '246 publication teaches compounds of its formula I that undergo tautomeric rearrangements, in which hydrogen from a ring enol moves to the adjacent nitrogen and back. These tautomeric forms exist because the enol-adjacent ring nitrogens are unsubstituted. Such tautomeric rearrangements are well known and

understood by those skilled in the art. *See Declaration Under 37 C.F.R. §132 of Michael Rowley, paragraph 10 (attached).*

Tautomeric rearrangements such as those taught by the '246 publication, do not occur when the nitrogen atom to which the H migrates during tautomerization is substituted. *See Declaration, paragraph 11.* The '246 publication discloses only tautomeric compounds and does not suggest providing a substituent that would block such tautomerization. *See Declaration, paragraph 12.* Thus, the claimed compounds are distinct from and patentable over the compounds disclosed in the '246 publication.

Further, the claimed compounds, which are R<sup>1</sup> substituted at the ring nitrogen adjacent to the ring carbonyl, provide distinct advantages that are not obvious over the tautomeric compounds of the '246 publication. *See Declaration, paragraph 13.* Exemplary compounds have been prepared and tested, and these compounds show unexpected advantageous properties over similar tautomeric compounds. In particular, the exemplary compounds according to the claims demonstrated improved bioavailability with at least comparable inhibitory concentrations, when compared to structurally similar tautomeric compounds as disclosed in the '246 publication. *See Declaration, paragraphs 14-18.* Improved oral bioavailability of such claimed compounds is an unexpected benefit of the claimed compounds.

The '246 publication does not provide any motive to inhibit the tautomerization of its compounds and in particular does not teach or suggest alkyl substitution of its ring nitrogens. For at least this reason, the '246 publication does not teach or suggest the compounds of claim 1 and its dependent claims.

Accordingly, claim 1 and its dependent claims are not obvious over the '246 publication. Reconsideration and withdrawal of the rejection are respectfully requested.

### **III. Double Patenting**

Claims 1, 3-9 and 14 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1-7 and 9-15 of U.S. Patent No. 7,091,209 to Gardelli et al., which is assigned to Istituto Di Ricerche Di Biologica Molecolare P Angeletti SPA, a wholly owned subsidiary of Merck & Co., Inc. While Applicants do not necessarily agree with this rejection for at least the same reasons discussed above with respect to the

'246 publication, a terminal disclaimer in compliance with 37 C.F.R. §1.321 is filed herewith. Reconsideration and withdrawal of the rejection are respectfully requested in light of these amendments.

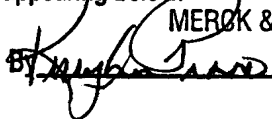
**IV. Conclusion**


In view of these amendments and arguments, Applicants respectfully submit that this application is in condition for allowance. The Examiner is invited to contact the undersigned at the telephone number set forth below, should he believe that anything further is necessary to place this application in even better form for allowance.

Please charge Deposit Account No. 13-2755 for any fees due in connection with this Amendment. If any time extensions are needed for the timely filing of this Amendment, Applicants petition for such extensions and authorize the charging of Deposit Account No. 13-2755 for the necessary fees.

Respectfully submitted,

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date appearing below.

BY  Date 24/Sept./2017  
MERCK & CO., INC.

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Date September 24, 2007

Attachments: Petition for Extension of Time  
Notice of Appeal  
Declaration Under 37 C.F.R. 1.132  
Terminal Disclaimer